Off-label use of tofacitinib: a potential treatment option for SAPHO syndrome

Synovitis, acne, pustulosis, hyperostosis and osteitis (SAPHO) syndrome is a rare and often under-reported autoimmune disease, characterised by prominent cutaneous and articular inflammation.¹ SAPHO syndrome is initially classified within spondyloarthritis, whereas recent evidence indicated that it is preferable as a primitive inflammatory osteitis. There are currently no formal evidence-based guidelines regarding the management of SAPHO syndrome, although variable degrees of efficacy of pharmacological therapies have been previously described, including non-steroidal anti-inflammatory drugs, glucocorticoids, disease-modifying antirheumatic drugs, bisphosphonates and even antibiotics.² Moreover, antitumour necrosis factor (TNF), interleukin (IL)-1 receptor antagonist also showed beneficial effect to the refractory SAPHO patients.³ Nonetheless, treatment failure or paradoxical effect is still frequent in daily practice.

Tofacitinib is a potent, Janus kinase (JAK) 1/3 inhibitor, which has been approved to treat immune-mediated diseases (IMDs), including rheumatoid arthritis, psoriatic arthritis and ulcerative colitis.⁴ In light of the important pathogenic role of the JAK/signal transducer and activator of transcription (STAT) pathway in IMDs, tofacitinib is being increasingly off-label used for the rheumatic diseases, especially for conditions refractory to currently standard treatment algorithms, including dermatomyositis/polymyositis, systemic sclerosis, systemic lupus erythematosus.⁵ Most recently, a pilot study conducted by Li *et al* from Peking Union Medical College Hospital, in which worldwide largest cohort of SAPHO patients have been established since 2004, retrospectively, analysed the efficacy of tofacitinib 5 mg two times per day in 12 female patients with SAPHO syndrome.⁶ Overall, significant multidimensional improvements were observed regarding pain, skin lesions, systemic inflammation, quality of life and remission on MRI. Of note, tofacitinib 5 mg two times per day was also beneficial for patients with an inadequate response to anti-TNF or bisphosphonates.

The understanding of SAPHO syndrome remained extremely stagnant. Recent studies revealed the potential role of cytokine dysregulation, such as TNF- α , IL-1 β , IL-8, IL-17 and IL-18.²⁻⁹ The effectiveness of tofacitinib would be expected to be associated with its potent and broad suppression of cytokine network via direct and indirect manner. In addition, tofacitinib has been documented to suppress osteoclast-mediated bone resorption by inhibiting the receptor activator for nuclear factor κ B ligand (RANKL) pathway.¹⁰ The efficacy of tofacitinib strongly suggested the role of JAK-STAT signalling pathway in the pathogenesis of SAPHO syndrome. Li's study indeed provides an important therapeutic option for refractory SAPHO patients who have failed with biologics therapies, but further observation is needed due to the limitations in design and sample size. Furthermore, identifying characteristics of patients and disease subtypes which may hint benefit from tofacitinib therapy deserves consideration in the setting of the complexity and heterogeneity of SAPHO syndrome.

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